# Lymphocytes subsets after one year of dimethylfumarate treatment in multiple sclerosis: a real life study.

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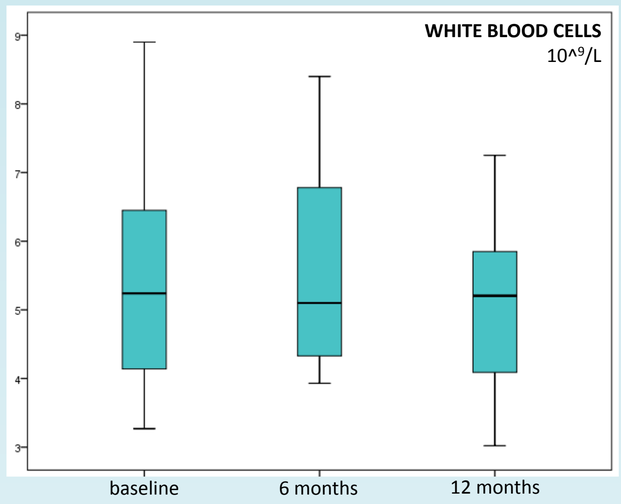
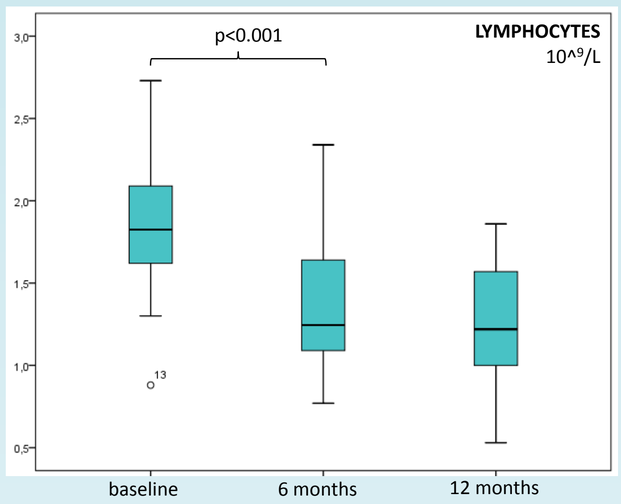
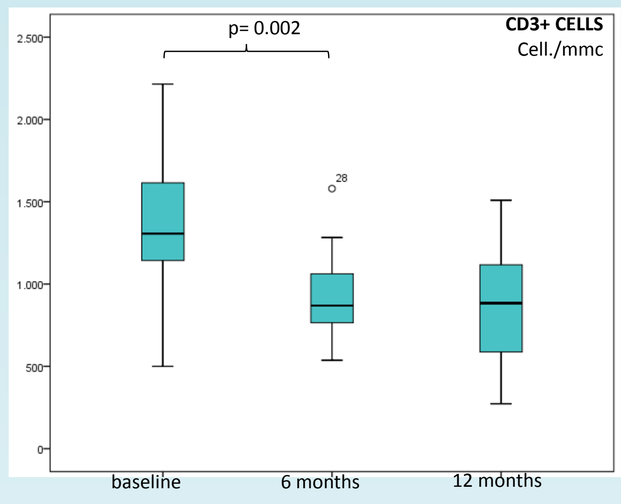
**OBJECTIVES**: Dimethylfumarate (DMF) is used to treat relapsing multiple sclerosis and causes lymphopenia in a subpopulation of patients. Much remains to be understood about how the drug affects lymphocyte subsets. Our objective was to characterize changes in lymphocytic phenotype induced by DMF and if these changes are transient or persistent after 1 year of treatment.

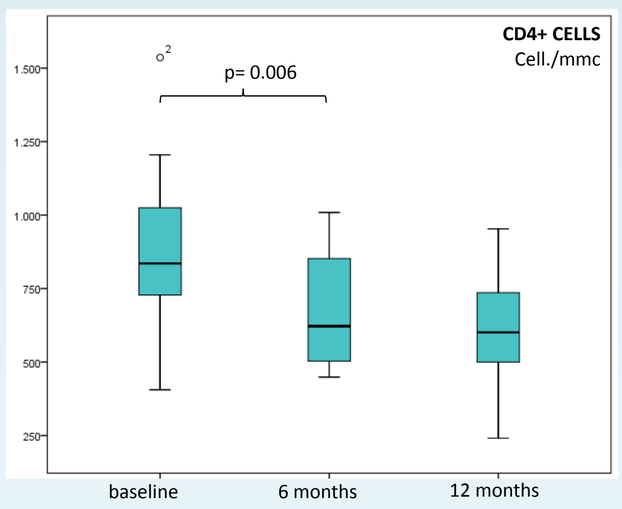
**MATERIALS**: Blood samples.
**METHODS**: Peripheral blood samples were collected from 38 consecutive DMF-12 months-treated patients at our multiple sclerosis center at 3 different time points: before treatment start, after 6 months and 12 months of DMF treatment. Leucocytes count, lymphocytes count and lymphocyte subsets (CD3+, CD4+, CD8+, C20+ and NK cells) were analyzed by flow cytometry, CD4/CD8 ratio was also evaluated.

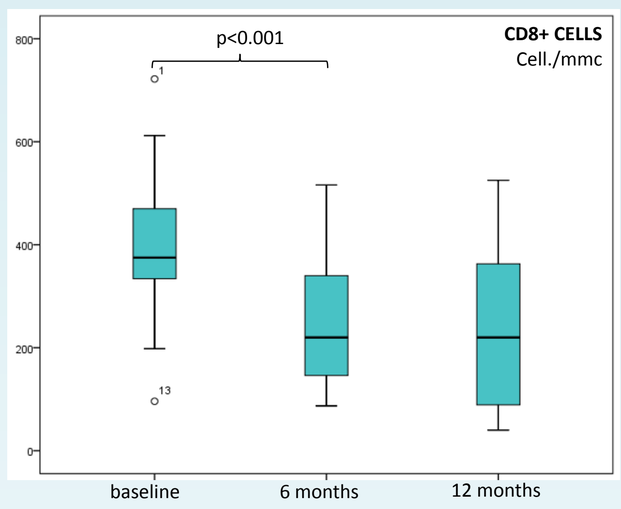
**RESULTS:** The total leucocytes count resulted unaffected by treatment. Lymphocyte count was significantly lower after 6 months of DMF treatment with persistent lower levels after 12 months (mean: 1.83 10^9/L pre-treatment, SD 0.46; 1.31 after 6 months, SD 0.51; 1.21 after 12 months, SD 0.40; p<0.001). All lymphocytes subsets, apart from NK cells, resulted significantly affected by treatment. CD3+ cells were significantly lower after 6 and 12 months of DMF (1448 cells/mmc, SD 569; 848, SD 311; and 810, SD 325; p=0.002). CD4+ cells were significantly lower after 6 and 12 months of DMF as well (922 cells/mmc, SD 352; 606, SD 207; 567, SD 201; p=0.006). CD8+ cells were the more affected subset, significantly lower at 6 and 12 months (481 cells/mmc, SD 239; 229, SD 130; 229, SD 140; p<0.001). C20+ cells were also mildly affected (290 cells/mmc, SD 181; 189, SD 107; 191, SD 83; p=0.044). A significantly higher CD4/CD8 ratio at 6 and 12 months (2.16, SD 0.74; 3.3, SD 1.6; 3.3, SD 1.8; p<0.001) was detected.

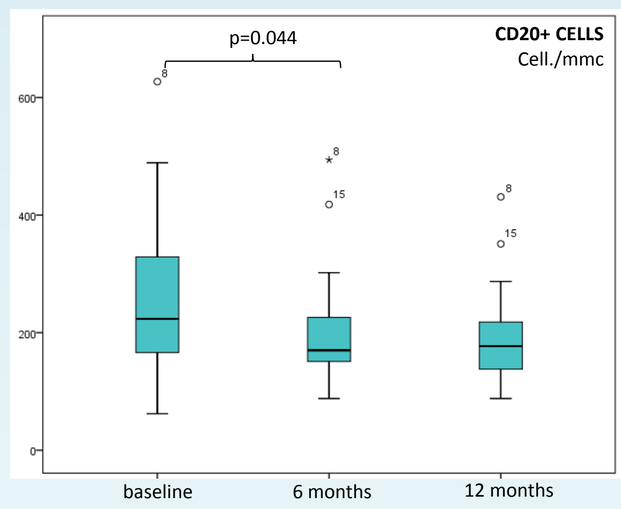


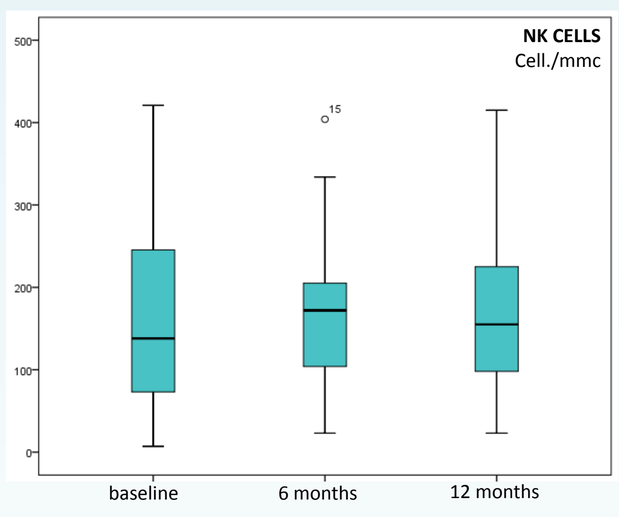



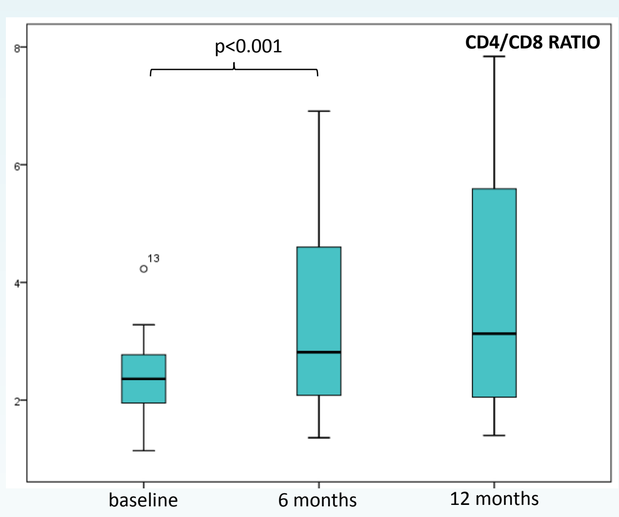




**DISCUSSION**: The results of our real life study, though small, are consistent with those previously reported at 6 months and confirm the lowering of lymphocyte levels as an effect of DMF. CD8+ cells seem to be the more affected subset.

**CONCLUSION**: Lymphocytes subsets changes are confirmed at 12 months, implicating a persistent alteration of the immune cellular profile under DMF treatment, which may be clinically relevant. Much remains to understand if these changes may be considered surrogate markers for efficacy and if safety implications have to be raised due to relative immunosuppression.

**References:**

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